



A NOTE ON "MULBERRY CELLS" AND CLUSTERS OF EOSINOPHILE SPHERULES, PROBABLY A FORM OF RUSSELL'S "FUCHSINE BODIES" IN THE WALLS OF A CHRONIC CEREBRAL ABSCESS AND IN A CASE OF MULTIPLE MYELOMA.

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(PLATE III.)

The subject of the chronic cerebral abscess was a married woman, æt. 37, admitted into the German Hospital on 13th October 1904. She had suffered from occasional headaches (since Christmas 1903) and vomiting; but, though she felt weak, had been up and about until three weeks before admission. No history of fits or convulsions. Some years previously she had suffered from spasmodic abdominal pains, possibly connected with cholelithiasis. In regard to family history, it may be noted that her father lived to an old age and her mother died of consumption. The patient had five children living and healthy; two others had died, of diphtheria and some uncertain cause,

respectively.

In the hospital the patient was found to have advanced double optic neuritis. The pupils were rather large, and reacted sluggishly to light. Though there was no objective disturbance in the movements of the eyeballs, diplopia of some kind was mentioned by the patient. There was no paraplegia, but without assistance she could not remain in the standing position, even with her eyes open, and she had a tendency to fall to the right. No disturbance of cutaneous sensation was detected, but there was apparently slight inco-ordination in the upper extremities, shown by asking her to make the tips of her two forefingers meet rather quickly in front of her. She answered even the simplest questions slowly. We have no note as to the condition of the knee-jerks and other reflexes. Nothing abnormal was observed on physical examination of the thorax and abdomen. There was no fever. The pulse varied between 76 and 88 per minute. The urine was free from albumin and sugar. The patient died suddenly in the night on 22nd October. Treatment by iodide of potassium had been commenced on the chance of the disease being due to syphilis.

At the necropsy on 22nd October nothing abnormal (spinal cord not examined) was discovered on naked-eye examination, beyond the presence of gall stones in the gall bladder and a chronic abscess (? softening gumma) in the brain. It is to this latter condition we have now to devote our attention.

The abscess was of about the size of a large walnut, measuring nearly 4 cms. in the sagittal direction and about $2\frac{1}{2}$ cms. in the coronal and vertical directions, and was situated in the left cerebral hemisphere, just above the corpus callosum and quite close to the intercerebral fissure, so as to cause bulging when the hemispheres were separated. There was a thrombosed blood vessel

in the cerebral cortex in the neighbourhood of the abscess. In this macroscopic examination of the brain we had the advantage of Dr. F. E. Batten's kind assistance. The other portions appeared not to be diseased, and this would account for the absence of localising symptoms during life. The abscess contained a thick, creamy, greenish, purulent-looking fluid, which under the microscope was found to consist of granular material and cells, the latter relatively few and in process of degeneration. The abscess wall was firm and rather irregular, and this irregularity rather favoured the view that the disease was of syphilitic origin. It may be stated at once that sections were specially stained for tubercle bacilli with a negative result.

MICROSCOPICAL EXAMINATION OF THE ABSCESS WALL.

Sections cut from paraffin blocks were stained in various ways. By the mode of preparation all fat was of course necessarily got rid of. The tissue was fibroid, with inflammatory cellular infiltration, merging on the outer side into normal brain tissue. Besides lymphocytes there were a good many rather large cells of an oval shape, which evidently, as the result of a degeneration process, had an extremely small nucleus and a relatively large amount of swollen-looking protoplasm, staining poorly with hæmatoxylin. It is, however, to a third kind of cells, representing, doubtless, a special form of degeneration, to which we particularly wish to draw attention. These cells, scattered here and there in the abscess wall, were of large size, with a single relatively small nucleus, and contained spherical globules (Plate III. Figs. 2 and 3) in their protoplasm, up to fifteen or twenty in number.

The spherules attracted attention owing to their retaining the fuchsine colour in preparations which were stained with carbol-fuchsine for tubercle bacilli, but they were likewise picked out by the eosine in the ordinary hæmatoxylin-eosine staining, and could be well defined by several other methods. On account of their peculiar appearance we have called the cells containing the globules "mulberry cells." It seems as if after a time the protoplasm becomes quite used up in the formation and growth of these globules, so that the cells come to consist of nothing but a small irregularly shaped nucleus and a mass of spherules apparently held together by a kind of cement substance or by a thin cell wall (Plate III. Fig. 3). Then, as far as we can judge, the nucleus disappears, and nothing but a cluster of spherules remains (Plate III. Fig. 1), or the cell breaks and the spherules are set free in the tissue; but even after this their arrangement in a group or cluster, and the appearance of adherence of some of the spherules to each other, often still suggest that they have been derived from the breaking up of a single mulberry cell. In the lowest of the three clusters represented in Plate III. Fig. 1, a small body, stained deep blue, is to be noted between the spherules, and appears to be the atrophied remnant of a nucleus, as if the cluster in question had been derived from a mulberry cell similar to that represented in Fig. 3.

The diameter of the spherules in the mulberry cells and clusters is mostly from one-sixth to rather more than the whole diameter of an ordinary redblood corpuscle. That is to say, that in diameter the spherules mostly vary between 1.5 and 9 or 10 μ , but are sometimes decidedly larger, especially when only one or two are contained in a single cell. Some of the spherules at first sight appearing to be free in the tissue are, on careful examination, found to be single globules, replacing, practically, the whole of the cell protoplasm, though a remnant of the nucleus is left. When many spherules are, as is usually the case, contained in the same cell, they often vary considerably in size. The spherules seem all to be perfectly homogeneous, and we can make out no vestige of structure in any of them. The larger ones stain, if anything, more deeply with eosine than the smaller ones.

We may note incidentally that in some preparations the large spherules apparently lying free in the tissue are a more striking feature than in other preparations, and we have a suspicion that the method of preparation may sometimes break up the cells, setting the spherules free, or may cause smaller globules to coalesce to form single large globules, either within cells or free in the tissue.

In regard to the staining reactions of the spherules, the following are our results from the use of a variety of stains:—

- 1. Hæmatoxylin and eosine—the globules are stained red.
- 2. Methylene-blue and eosine—red.
- 3. Jenner's methylene-blue and eosine combination 1—faint red.
- 4. Mann's long method of staining by his methyl-blue and eosine combination 2—red.
- 5. Ehrlich's triacid blood stain—crimson.
- 6. Methyl-violet—violet (i.e. not the pink staining of amyloid substance).
- 7. Carbol-fuchsine—red.
- 8. Fuch sine and methylene-blue—purple.
- 9. Russell's fuchsine and iodine-green method 3—red, often with a bluish tinge; sometimes, probably owing to faulty technique—blue.

It must be added that the spleen and a kidney from the same case were examined microscopically. Nothing abnormal was seen in the section of the kidney, but an interesting fact is that a few clusters of spherules, similar to those found in the walls of the cerebral abscess, were discovered in sections of the spleen. The latter organ showed no amyloid change, but a hyaline-like degeneration in the walls of some of the smaller blood vessels.

The mulberry cells and spherule clusters in the present case are obviously very similar to those found in greater abundance in the myelomatous bone marrow of a case described by one of us (F. P. W.) and illustrated in the *Mcdico-Chirurgical Transactions*, vol. lxxxvi.⁴ Professor R. Muir of Glasgow, who kindly examined the tissue in that case, reported:—

"In the protoplasm, moreover, there can be shown a larger number of granules which vary considerably in size, but the smallest and most abundant of which are distinctly larger than the neutrophile granules. With hæmat-

¹ Louis Jenner, Lancet, London, 1899, vol. i. p. 370.

² G. Mann, "Physiological Histology," 1902, p. 216.

³ W. Russell, "An Address on a Characteristic Organism of Cancer," Brit. Med. Journ., London, 1890, vol. ii. p. 1356.

⁴ F. Parkes Weber, "A Case of Multiple Myeloma," Med.-Chir. Trans., London, 1903, vol. lxxxvi. pp. 395 et seq.

oxylin and eosine these smallest granules are practically unstained by the eosine; with Ehrlich's triacid they are coloured, but have not quite the same tints as the nentrophiles, the staining being of a dirty brown colour; with Mann's eosine-methyl-blue combination they are stained bright red with a slightly violet tint (whereas the neutrophiles are not stained); with Unna's polychrome methylene-blue the granularity is faintly visible, but the granules are not really stained. . . . In addition, however, to these small granules, many larger ones are present, and all intermediate sizes can be found up to large rounded bodies as large as, or even larger than, ordinary red corpuscles. I thought at first that these rounded bodies were included red corpuscles. . . . Some of them also are seen lying free. They are more distinctly oxyphile than the smaller granules, and stain with eosine by the ordinary methods. . . . They always seem to be perfectly spherical in form." In the account of the case Dr. Weber added that some of the larger globules were two or three times as large as ordinary red eorpuscles. The globules of about the same size as red corpuscles were, however, more numerous, and were mostly enclosed in eells (Plate III. Fig. 4) or arranged in clusters as if those of each cluster had been formed in a single cell and were still held together in some way. Such clusters often eonsisted of a dozen or more globules, and sometimes resembled mulberries (Plate III. Fig. 5) or bunches of grapes.

Unfortunately, when we recently endeavoured to try fresh stains on sections of a piece of the myelomatous bone marrow which had been preserved in glycerin and formalin, we found that the tissue had undergone some change, so that the globules could no longer be properly stained. However, we believe it is clear that the globules, whether enclosed in mulberry cells or lying free in the tissue, were similar, if not quite identical, in their chemical nature in the two cases.

Mulberry-like cells, similar in form if not in their staining reactions, have been described and figured by Gulland and Goodall in their elaborate paper 1 on pernicious anæmia. In their cases of pernicious anæmia they found basophile cells with very large "dropsical-looking granules" in the intestinal submucosa. "Every intermediate stage," they said, "from the cell with ordinary granules to those with granules larger than erythrocytes, could be seen."

Mr. S. G. Shattock kindly suggested to one of us that the spherules in our cerebral abscess case might be allied to the so-called fuchsine bodies originally described by W. Russell ² as cancer organisms. Ruffer and Walker ³ say:—

"By means of a special stain he (W. Russell) showed that these fuchsine bodies occurred in little clusters of one up to twenty or more. They formed perfect spheres, and varied in size from 4 to $12~\mu$. They appeared to be perfectly homogeneous and structureless, and the larger elumps were held together by a delicate cementing substance, which stained faintly."

So much does this description tally with what we have observed in regard to the spherules and mulberry cells of our cerebral abscess

³ M. A. Ruffer and J. H. Walker, "On some Parasitic Protozoa found in Cancerous Tumours," Journ. Path. and Bacteriol., Edin. and London, 1893, vol. i. p. 200.

¹ Journ. Path. and Bacteriol, Edin. and London, 1905, vol. x. pp. 125 et seq. W. Russell, "An Address on a Characteristic Organism of Cancer," Brit. Med. Journ., London, 1890, vol. ii. p. 1356.

case, that we think the spherules in the latter case may certainly be regarded as a form of Russell's fuchsine bodies. We say advisedly "a form of," because it is possible that Russell's "fuchsine bodies" are not all exactly identical with each other.

It follows from all this that the spherules found in Weber's multiple myeloma case, to which we have already alluded, though present in extraordinary abundance both in clumps within the cells (sometimes in the form of mulberry cells) and scattered free in the tissues, must likewise be regarded as probably forms of Russell's fuchsine bodies, in spite of the fact that they were never tested by Russell's fuchsine and iodine-green method of staining.

The importance of this conclusion lies partly, we believe, in the fact that, since fuchsine bodies are now regarded by almost all observers merely as products of cell degeneration, they are not likely to possess any special pathological diagnostic significance in regard to multiple myeloma, and it is unlikely that they are more closely connected with multiple myeloma (and Bence-Jones' albumosuria) than with other conditions in which they have been found present. This is confirmed by the fact that their presence has not been recorded in most other published cases of multiple myeloma.

DESCRIPTION OF PLATE III.

Fig. 1.—Part of the wall of the chronic cerebral absecss showing clusters of the spherules stained red. Mann's long method of staining by his cosine and methyl-blue combination. (High magnification.)

Fig. 2.—From another section of the abseess wall. Two eells containing a great number of relatively small spherules stained purple by Russell's fuelsine and iodine-

green method. (High magnification.)

Fig. 3.—From another section of the abseess wall. A mulberry cell in which the protoplasm has been apparently entirely replaced by the spherules. Eosine and hæmatoxylin stain.

Fig. 4.—From the multiple myeloma ease. A granulated eell containing spherules of various sizes stained red by Mann's cosin and methyl-blue combination. A somewhat diagrammatic representation, reproduced from the *Med.-Chir. Trans.*, London, vol. lxxxvi.; but the blue colour of the nucleus in the present illustration is more correct than that in the original figure.

Fig. 5.—From the multiple myeloma ease. A mulberry cell in which the protoplasm has been apparently entirely replaced by spherules of various sizes. The nucleus is still visible. Mann's cosine and methyl-blue stain with hæmatoxylin. Figure reproduced from the Med.-Chir. Trans., London, vol. lxxxvi.

¹ Vide Shattoek and Ballanee, Brit. Med. Journ., London, 1891, vol. i. p. 565, and many later observers. Recent workers in Germany, we believe, regard Russell's fuelsine bodies as representing a form of hyaline degeneration.

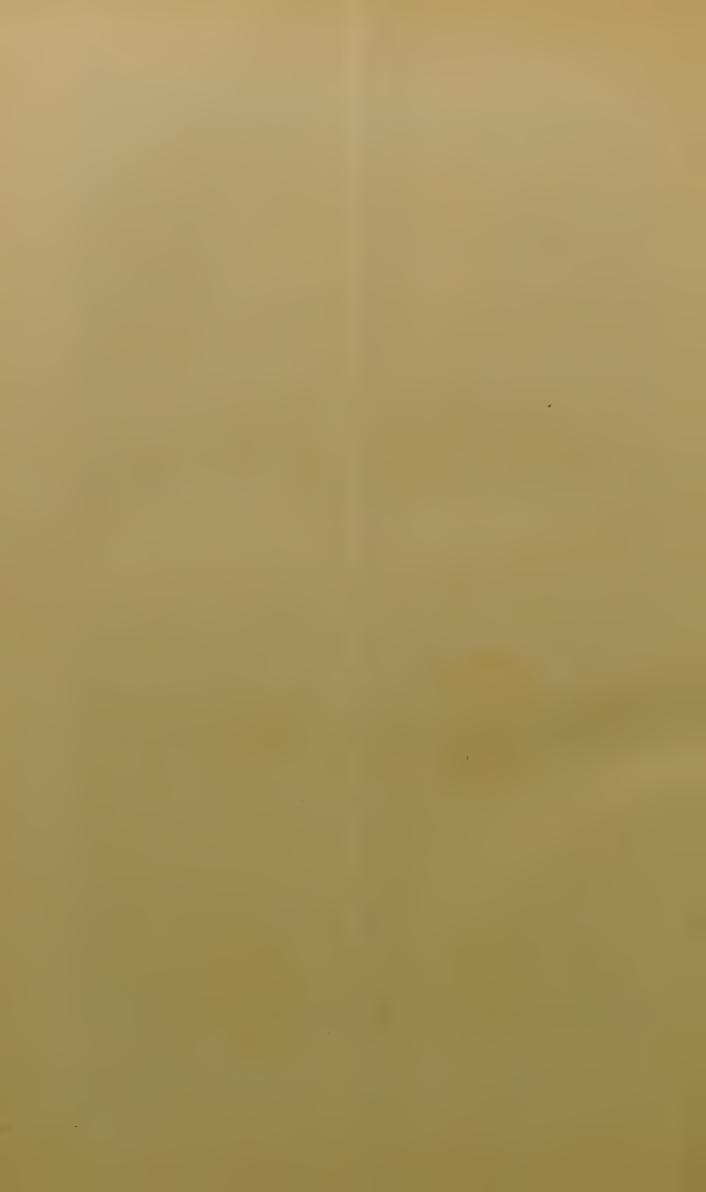
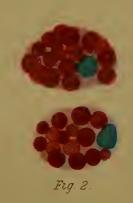




Fig I





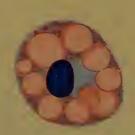


Fig 4.







